"Formulation of nanocapsules of methyl eugenol & terpineol and comparison of their neuroprotective activity."

A proposed synopsis/ Research proposal of Dissertation Submitted to

Jayoti Vidyapeeth Women's University - [JVWU], Jaipur

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SUBMITTED BY

Ms.Pradnya Karbhari Pehere

(Research Scholar)

UNDER GUIDANCE OF

JV'n Prof. DR. DHANMEDRA AHUJA

(Dean, Faculty of Pharmaceutical Sciences)

Jayoti Vidyapeeth Women's University - [JVWU], Jaipur

Title- "Formulation of nanocapsules of methyl eugenol & terpineol and comparison of their neuroprotective activity."

1. Introduction:

Polymer-based nanocapsules have been widely studied as a potential drug delivery system in recent years. Nanocapsules—as one of kind nanoparticle—provide a unique nanostructure, consisting of a liquid/solid core with a polymeric shell. This is of increasing interest in drug delivery applications. In this review, nanocapsules delivery systems studied in last decade are reviewed, along with nanocapsule formulation, characterizations of physical, chemical, biologic properties and applications. Furthermore, the challenges and opportunities of nanocapsules applications are also proposed. However, non-biodegradable, but biocompatible polymers such as polyethylene glycol (PEG), polyvinyl alcohol (PVA) have also been widely used to contribute to the fabrication of nanoparticles.

Therefore, proposed study focuses to find out simple, economic, best, efficient processing technologies for the improving the API solubility, dissolution rate, potentially the intestinal permeability and bioavailability by using nanocapsules formulation.

The Nano encapsulation of essential oil has been greatly important in different dosage form, given its remarkable antioxidant and antimicrobial capacity. However, its analysis in storage has not been established in terms of physical stability, neuroprotective capacity, and release studies.

Rationale of herbal medicine

1. Low/Minimum cost
2. Complete accessibility
3. Enhanced tolerance
4. More protection
5. Fewer side-effects
6. Potency and efficiency is very high.

2. Literature Review:

1. Bantu Karnakar, et.al. (2021)

Bantu Karnakar studied a range of nano-dimensional materials, including Nano robots and Nano sensors that are applicable to diagnose, precisely deliver to targets, sensor activate materials in live system have been outlined. Study report that Nanocapsules, existing in miniscule size, which range from 10 nm to 1000 nm. They consist of a liquid/solid core in which the drug is placed into a cavity, which is surrounded by a distinctive polymer membrane made up of natural or synthetic polymers. They have great interest of attraction because of the protective coating, which are usually Pyrophoric and easily oxidized and delay the release of active ingredients. Various technical approaches are utilized for obtaining the Nanocapsules however, the methods of interfacial polymerization for monomer and the Nano deposition for preformed polymer are chiefly preferred.

2. Joslaine Jacumazo et. al., (2023)

Joslaine Jacumazo et. al.,were reported that eugenol-loaded nanocapsules Ne formation is an important step to obtain nanocapsules since it was used as a template for the LbL process this work, the variation of the sonication time to obtain the Ne was evaluated. Droplet size and the polydispersity index (PDI) of the Ne as a function of sonication time are shown in Figure 1a. After 240 s of sonication, there is a decrease in the droplet size and sample dispersion ($p < 0.05$) in the dispersion due to the greater amount of energy supplied to the system Figure 1b. PDI < 0.250 suggested a more homogeneous distribution, reducing the Ostwald ripening and contributing to stability. In this context, the best condition to form homogeneous Ne droplets was determined at 600 s of sonication.

3. Maribel Teixeira, et.al. (2004)

Maribel Teixeira et. al., adopted the solvent displacement technique in this work was found to be appropriate for the preparation of nanoparticle formulations containing either XAN or 3-MeOXAN. This process allowed us to obtain nanospheres of a mean diameter! 170 nm and nanocapsules of a mean diameter! 300 nm. Nano incorporation of these poorly water-soluble compounds affords the preparation of formulations with higher concentrations of XAN or 3-MeOXAN than those corresponding to the respective aqueous solutions. Nanocapsules appear to be more appropriate carriers for both xanthones, once encapsulated XAN and 3-MeOXAN concentrations in the final dispersions were 60 and 100-fold, respectively, to those corresponding to nanospheres. 3-MeOXAN release from nanocapsules is governed mainly by its partition between the oil core and the external aqueous medium. The release profile of XAN

from nanocapsules suggests the existence of an interaction of the drug with the polymer. Developed nanocapsule formulations were shown to be physically stable for a period of 3–4 months.

4. Siyuan Deng, Maria Rosa Gigliobianco et.al., (2020)

Research of polymeric nanoparticles has widely attracted attention recently. This mini review has reported the studies and progress of polymeric nanocapsules as drug delivery system in pharmaceutical field, in last decade. To perform the specific core-shell nanostructure, various materials were used for polymeric nanocapsule formulation via the interfacial deposition method, nano-emulsion template method or lay-by layer method. The selection of polymers and formulation methods mainly depends on the characteristics of pharmaceutical ingredient and application purpose. Polymeric nanocapsules as drug delivery systems can improve the bioavailability of payloads and achieve sustained and targeted delivery. Additionally, future perspectives in polymeric nanocapsules should focus on studies of using new and most performing polymers to develop advanced delivery system, thereby extending the applications of polymeric nanocapsules in pharmaceutical fields.

5. Lorena de Oliveira Felipe et.al., 2021

In this study Lorena de Oliveira Felipe et.al., were showed that α-TOH may act as a co-surfactant due to its ability to lower the interfacial tension on the oil-water interface in the absence or presence of surfactant into the aqueous solution. The long-term stability tracked from 0 to 410th day for 9αTOH-NE loaded with high-amount of α-TOH (90 mg mL−1), showed some key-findings: (i) the preparation of this nanocolloidal system by high-pressure homogenizer did not cause degradation to the initial amount of α-TOH added for its O/W nanoemulsion formulation; (ii) despite the high-susceptibility of α- TOH to degradation depending on temperature, moisture, and air exposition, the chemical stability of this sensitive bioactive ingredient was extended over than 1-year through its nanoemulsion Formulation.

6. Dheebika Natarajan, et.al.,(2015)

Dheebika Natrajan et.al., focuses the study on developing a CS-AL nanocarrier for the encapsulation of essential oils. The effects of process parameters such as the effect of heat and the concentrations of AL and CS were investigated. Various physicochemical characterization techniques such as scanning electron microscopy, Fourier transform infrared spectroscopy, and ultraviolet visible spectroscopy were performed. Results of characterization studies showed

that 0.3 mg/mL AL and 0.6 mg/mL CS produced minimum-sized particles (<300 nm) with good stability.

The antiproliferative activity of essential oil-loaded nanocapsules was estimated using MTT assay and it was found that the activity of turmeric oil is retained in the carrier. The carrier showed high cell viability percentage, which indicates that it is nontoxic. It was also confirmed from the clear supernatant in haemolysis assay that our oil-loaded nanocapsules were hemocompatible, which suggests that they are a suitable carrier for further biomedical applications.

7. Wei Liao, Waisudin Badri et.al., (2021)

In this case, natural antibacterial agents, such as essential oils, have the potential to provide quality and safety benefits and have a reduced impact on human health, but they still have some drawbacks. The advancements in nanotechnology can protect active compounds from degradation, improve their solubility, and control their release compared to adding the antimicrobial agent.

8. Ubonphan Rodsuwan et.al., (2020):

Ubonphan Rodsuwan et.al reported the Gamma API (GO), a bioactive ingredient found in rice bran oil, for a variety of biological effects such as antioxidant activity, reduction of total cholesterol, anti-inflammation, and antidiabetic. A nano-encapsulation technique was investigated to improve its stability and quality. In this research, gamma API was successfully encapsulated into zein nanoparticles. The fabrication parameters including pH, zein concentration (0.3, 0.4, and 0.5% w/v), and % GO loading (30, 40, and 50% by weight) were investigated. Particle size, zeta potential, yield, encapsulation efficiency and the stability or GO retention during the storage were determined. The morphology of gamma API loaded zein nanoparticles (GOZNs) was observed by scanning electron micrographs and transmission electron microscope. The increase of zein concentration and % GO loading resulted to an increase of yield, encapsulation efficiency, and particle size. The particle size of the GOZNs ranged from 93.24–350.93, and 144.13–833.27, and 145.27–993.13 nm for each zein concentration with 3 loading levels, respectively. Nano-encapsulation exhibited higher % GO retention compared with nonencapsulated GO during 60 days storage both at 4°C and −18°C. In vitro study indicated the sustained release of GO in the simulated gastric fluid followed by simulated intestinal fluid. This finding indicated a high potential for the application of insoluble GO with improved stability by encapsulation with the hydrophobic zein protein.

9. Hatem Ali et. Al., (2020)

In this study Hatem Ali find that the volatiles composition of the oil nanoemulsion was found to be dramatically different from that of the hydrodistilled oil. In the oil nanoemulsion, α-terpineol (35.68%), borneol (34.29%) and Thymol (13.47%) were identified as the major constituents. This study investigated the effect of nanoencapsulation on the composition of volatile compounds, as well as the antioxidant and anticancer activities of hydrodistilled (HD) *Origanum glandulosum* Desf. Oil, which was encapsulated into nanocapsules via High Speed Homogenization (HSH) and into nanoemulsions through High Pressure Homogenization (HPH). Thirty-two volatile components were identified using Gas Chromatography-Mass Spectrometry analysis (GC-MS) in HD essential oil representing 99.04% of the total oil content. GC-MS analysis showed that the use of HPH to prepare nanoemulsions negatively affected the active compounds present in HD oil, particularly carvacrol and thymol, whereas the use of HSH led to significant quantitative differences in the composition of volatiles between HD oil and nanocapsules but generated the same profile.

10. Arpita Samanta, et.al. (2016)

Arpita Samanta et.al., discuss in this article about the development of a biodegradable nanoparticle formulation of CH based on PLGA technique using DMAB as a stabilizer and tested its bioavailability and efficacy on rats where we found that nanocapsulated catechin hydrate [NPCH] and nanocapsulated catechin hydrate-sodium meta borate [NP (CH+SMB)] had much higher cellular uptake *in vitro* compared to that of free catechin hydrate. However identical cellular uptake was noticed for both the cases. This method has been used to encapsulate a wide variety of hydrophobic drugs including coenzyme Q, ellagic acid, estradiol, taxol ellagic acid and camptothecin.

11. Mario D.L. Moretti et.al., (2002)

Mario D.L. Moretti et.al.,studied in this research encapsulation process is a suitable method for entrapping essential oils of a very different chemical composition. This method reduces loss of the active principles, leading to high-loaded microparticles that offer protection against environmental agents; it also offers the possibility of controlled drug release. Data obtained in the release tests show that loss of active principles occurs when microcapsules are exposed to environmental humidity.

12. Ricardo M. González-Reza et.al., (2021)

The nano encapsulation of thyme essential oil has been greatly important in food science, given its remarkable antioxidant and antimicrobial capacity. However, its analysis in storage has not been established in terms of physical stability, antioxidant capacity, and release studies. In this paper, chitosan-thyme oil nanocapsules were prepared by the ionic gelation method. These were characterized for differential calorimetry, release kinetic, and infrared spectroscopy. The chitosan-thyme oil nanocapsules were stored at 4 and 25 0C for 5 weeks, the changes in particle size, zeta potential, stability (diffuse reflectance), and antioxidant capacity were analysed and associated with nanocapsules functionality.

13. Sonali G. Banpure et. al., (2022)

Sonali G. Banpure studied that a variety of natural products are used alone or in combination with other neuroprotective medicines, according to various experimental studies, to improve memory and comprehension in AD patients. Overall, this pioneering study was utilized to examine for the first time if compounds derived from natural products could be able to reveal the chemical binding mechanism. The standard case study research was also employed to assess the longest ligands. To understand how the medicine interacts with the symbolic macromolecule (11 AD target), it is crucial to understand the binding capacity of the drug interactions.

14. Shubham Tripathi et.al., (2018)

This study is further aimed to perform in vivo studies for analyzing the concentration of ketone bodies reaching into the brain and to study its effect in removing β amyloid plaque, which will help to reduce the dose of coconut oil emulsion and to make its novel dosage form for treatment of Alzheimer's disease.

15. Ion Brinza et.al.,(2021)

In this study Bay leaf (*Laurus nobilis* L.) has been shown to possesses various biological activities such as wound healing activity, antioxidant activity, antibacterial activity, antiviral activity, immunostimulant activity, anticholinergic activity, antifungal activity, insect repellent activity, anticonvulsant activity, antimutagenic activity, and analgesic and anti-inflammatory activity. The present study aimed to investigate whether the bay leaf incense (BL) elicits the memory formation via the action on the cholinergic system using a scopolamine (Sco)-induced rat model. Rats were exposed to BL over 5 min in a smoking chamber apparatus once daily for

22 days, whereas memory impairment was induced by Sco (0.7 mg/kg), a muscarinic receptor antagonist, delivered 30 min before each behavioural test.

16. Ioannis L. Liakos,et.al.,(2018)

In this study bioactive nano systems by combining cellulose acetate with three selected essential oils (EOs) to create spherical nanocapsules (NCs) using the Solvent /anti-solvent technique. The biological activity of the obtained NCs was promoted by the use of some antimicrobial EOs: Peppermint, Cinnamon and lemongrass which were grafted on the cellulose acetate molecules. Due to their chemistry, such as long hydrocarbon tails and heads with functional groups these EOs were playing also the role of surfactant-like substance facilitating the formation of NCs.

17. María Javiera Alvarez-Figueroa et.al. 2020

María Javiera Alvarez-Figueroa et.al. were made nanocapsule by solvent displacement method and their physicochemical properties was measured by DLS and laser-Doppler. For transdermal experiments, newborn pig skin was used. The Raman spectra were obtained using a laser excitation source at 532 nm and a 20/50X oil immersion objective.

18. Laura Marcela Forero Ramirez et.al. 2020

Laura Marcela Forero Ramirez aiming to prepare oily core pH-sensitive nanocapsules (NCs) for anticancer drugs delivery, the use of a dextran-based transurf (DexN3-sCTAc) as both stabilizer and macromolecular chain transfer agent in methyl methacrylate/2-(diethylamino) ethyl methacrylate (MMA/DEAEMA) miniemulsion copolymerization was investigated. NCs of about 195 nm with an oily-core of Miglyol 810 (M810) and a dextran coverage covalently linked to the poly(MMA-co-DEAEMA) intern shell have been obtained.

19. Xavier-Jr., F.H.et.al.,2020

New poly (isobutyl cyanoacrylate) based nanocapsules were synthesized by interfacial polymerization having a surface coated with chitosan. Paclitaxel could be incorporated in the nanocapsules, which cavity was filled out with copaiba oil, while chitosan conferred interesting mucoadhesive properties to the new formulation.

20. Natalia Prado da Silva et.al. , 2020

The present study resulted in a successful development of core-shell nanocapsules to improve the activity of TTO against C. acnes. The developed nanocapsules presented suitable physicochemical characteristics based on size, PdI, ZP, pH, and entrapment efficiency evaluation.

21. Muhammad Bilal, et.al. 2020

Muhammad Bilal, et.al. reported that nanoscience and nanotechnologies are evolving as one of the emergent technologies, which can open new horizons for exploring innovative solutions to circumvent and treat neurodegenerative diseases including Alzheimer's disease, Huntington's disease, Parkinson's disease, etc. A therapeutic implication in the number of researches expands to alter the therapeutic course of the AD at an enhanced rate.

22. Mukta Agrawal et. al., 2018

Mukta Agrawal et. al. reported in this article about Recent advancements in the field of nanotechnology for the delivery of anti-Alzheimer drug in the brain region Nano particulate drug carrier system offers most possible strategy with a variety of different forms and can easily modify to facilitate the drug targeting to eliminate various boundaries associated with it. The most common polymeric nanoparticle may be a good choice.

23. Prof. WANG Hui et.al.,2022

In this study Prof. WANG Hui reported that Nanocapsules Provide New Solution for Efficient Cancer Chemodynamic Therapy.It is a core-shell structure formed by ingeniously attaching a thin layer of carbon to the surface of hollow cuprous oxide (Cu2O) nanocrystals, which not only effectively prevents the oxidation 2 of Cu+, but also increases stability of Cu2O nanocrystals. Use for anti tumor activity.

24. Siyuan Deng, et al., 2020

In this review, nanocapsules delivery systems studied in last decade are reviewed,
along with nanocapsule formulation, characterizations of physical/chemical/biologic properties and applications. Furthermore, the challenges and opportunities of nanocapsules applications are also proposed. This mini review has reported the studies and progress of polymeric nanocapsules as drug delivery system in pharmaceutical field, in last decade. To perform the specific core-shell nanostructure, various materials were used for polymeric nanocapsule

formulation via the interfacial deposition method, nano-emulsion template method or lay-by layer method. The selection of polymers and formulation methods mainly depends on the characteristics of pharmaceutical ingredient and application purpose. Polymeric nanocapsules as drug delivery systems can improve the bioavailability of payloads and achieve sustained and targeted delivery. Likewise, they can also effectively reduce the harmful effects between payload and tissue environments.

25. Rafaela R. Ferreira et al., 2021

In this study Rafaela R. Ferreira et.al., were prepared PBAT films by the casting method. Different chitosan nanocapsules (CN-EO) content (2, 5, and 8 wt%) loaded with cinnamon essential oil (EO) were prepared and used as active agents in poly(butylene adipate-co-terephthalate) films. The prepared samples were characterized by chemical, physical–chemical, mechanical, and biological properties. The CN-EO presented monodispersed sizes from 20 to 100 nm and spherical shape. The nanocapsules showed biological activity due to the synergistic antibacterial efficiency of chitosan and essential oil, and when applied to the films, it promoted inhibition against E. coli

26. Renata Bem dos Santos et.al., 2022

Renata Bem dos Santoset.al., in this study aimed to develop nanocapsules (NCs) loaded with curcumin (CCM) using different coatings, comparing the effect of these coatings on physicochemical properties of NCs. NCs were prepared by interfacial deposition of performed polymer, using different polymers as coatings (P80, PEG, Chitosan and Eudragit RS100®) and then, characterized in detail by different techniques (AFM, FTIR, DSC, XRD, among others). In vitro studies were performed, evaluating the release profile, cytotoxicity and antimalarial activity of CCM-loaded NCs. Overall, all CCM-loaded NCs samples exhibited typical characteristics as nanometric size, coating-dependent zeta potential, acidic pH value, span values below 2, homogeneous morphology and CCM-distribution in pseudophases of type VI (for all of coatings).

27. Micaela Guidotti-Takeuchi , et al., 2022

Micaela Guidotti-Takeuchi , et al., provides an overview of EO-related nanosystems with application for different food matrices. The selection criteria of data were focused on the robust works that provided structural characterization of nanoparticles, physicochemical stability, and efficacy assays against food-related pathogens.

28. Giuseppe Granata, et.al.,2022

In this study Giuseppe Granata, et.al., formulate Fennel Essential Oil encapsulated into polymer-based particles using the interfacial deposition technique of preformed polymers. The encapsulation of FEO in PCL polymer nanocapsules was demonstrated by NMR.

29. G H Nguyen et.al., 2021

In this study, chitosan nanoparticles containing palmarosa essential oil (PEO-CNPs) were formed by ionotropic gelation, consisting of two parts: emulsion preparation followed by ionotropic gelation encapsulation with tripolyphosphate ions (TPP) as a crosslinker. The encapsulation method was optimized by varying three parameters, including chitosan concentration, initial oil loading in the emulsion and TPP concentration. The effects of these parameters on the encapsulation efficiency (EE) and loading capacity (LC) were analyzed. EE had an initial increase followed by a decrease in the range of three parameters.

30. Anju Bennyet.al., 2018

Aim of this review the relevant in vitro, in vivo, and clinical studies focused toward the potential uses of essential oils in the treatment of Alzheimer's disease. Clove oil is a mind stimulant used for medical care in anxiety, insomnia, and depression. The active constituents of its EO are eugenol (87.34%) and smaller amounts of eugenol acetate (5.18%) and β-caryophyllene (2.01%) [32].

EOs obtained from numerous medicinal plants are reported to possess anti-AD potential. EOs of S. officinalis, S. officinalis ssp. lavandulifolia (vahl), M. officinalis, L. angustifolia, and R. officinalis have proven their putative effects in clinical studies. EOs are rich in various bioactive markers in different concentrations and it changes from place to place

31. Natalia Prado da Silva et.al., 2020

Natalia Prado da Silva et.al was develop tea tree oil (TTO)-loaded chitosan-poly(ε-caprolactone) core-shell nanocapsules (NC-TTO-Ch) aiming the topical acne treatment. TTO was analyzed by gas chromatography-mass spectrometry, and nanocapsules were characterized regarding mean particle size (Z-average), polydispersity index (PdI), zeta potential (ZP), pH, entrapment efficiency (EE), morphology by Atomic Force Microscopy (AFM), and anti-Cutibacterium acnes activity. The main constituents of TTO were terpinen-4-ol (37.11 %), γ-terpinene (16.32 %), α-terpinene (8.19 %), ρ-cimene (6.56 %), and α-terpineol (6.07 %). NC-TTO-Ch presented Z-average of 268.0 ± 3.8 nm and monodisperse size distribution (PdI <

0.3). After coating the nanocapsules with chitosan, we observed an inversion in ZP to a positive value (+31.0 ± 1.8 mV).

32. Narimane Lammari et.al.,2020

In the present study, we investigated Saussurea lappa CB. Clarke. (SL) given its largely reported medicinal effects. Specifically, our objective was to provide an insight into a new polymethyl methacrylate based nanocapsules as carriers of SL essential oil and characterize their biologic functions. The nanoparticles were prepared by nanoprecipitation technique, characterized and analyzed for their cytotoxicity, anti-inflammatory, anti-Alzheimer and antidiabetic effects. The results revealed that the developed nanoparticles had a diameter around 145 nm, a polydispersity index of 0.18 and a zeta potential equal to +45 mV and they did not show any cytotoxicity at 25 $\mu g \cdot mL^{-1}$. The results also showed an anti-inflammatory activity (reduction in metalloprotease MMP-9 enzyme activity and RNA expression of inflammatory cytokines: TNF-α, GM-CSF and IL1β), a high anti-Alzheimer's effect (IC50 around 25.0 and 14.9 $\mu g \cdot mL^{-1}$ against acetylcholinesterase and butyrylcholinesterase, respectively), and a strong antidiabetic effect (IC50 were equal to 22.9 and 75.8 $\mu g \cdot mL^{-1}$ against α-amylase and α-glucosidase, respectively).

33. Nazeer Hussain Khan et.al., 2021

Nazeer Hussain Khan et.al., were studied that Alzheimer's disease (AD) is a devastating disease of the aging population characterized by the progressive and slow brain decay due to the formation of extracellular plaques in the hippocampus. AD cells encompass tangles of twisted strands of aggregated microtubule binding proteins surrounded by plaques. Delivering corresponding drugs in the brain to deal with these clinical pathologies, we face a naturally built strong, protective barrier between circulating blood and brain cells called the blood–brain barrier (BBB). Nanomedicines provide state-of-the-art alternative approaches to overcome the challenges in drug transport across the BBB. The current review presents the advances in the roles of nanomedicines in both the diagnosis and treatment of AD. We intend to provide an overview of how nanotechnology has revolutionized the approaches used to manage AD and highlight the current key bottlenecks and future perspective in this field. Furthermore, the emerging nanomedicines for managing brain diseases like AD could promote the booming growth of research and their clinical availability.

34. Angela Bonaccorso et.al., 2021

The aim of this work was the development of nanostructured lipid carriers (NLC) for the delivery of essential oils (*Lavandula*, *Mentha*, and *Rosmarinus*) by intranasal administration, an interesting topic in which Italian contributions have recently increased. Essential oil-loaded NLC, projected as a possible add-on strategy in the treatment of neurodegenerative diseases, were characterized in comparison to control formulations prepared with Tegosoft CT and Neem oil. Homogeneous (polydispersity index, PDI < 0.2) nanoparticles with a small size (<200 nm) and good stability were obtained. Morphological and physical-chemical studies showed the formation of different structures depending on the nature of the liquid oil component. In particular, NLC prepared with *Lavandula* or *Rosmarinus* showed the formation of a more ordered structure with higher cytocompatibility on two cell lines, murine and human fibroblasts. Taken together, our preliminary results show that optimized positively charged NLC containing *Lavandula* or *Rosmarinus* can be proposed as a potential add-on strategy in the treatment of neurodegenerative diseases through intranasal administration, due to the well-known beneficial effects of essential oils and the mucoadhesive properties of NLC. This preliminary study suggests that optimized positively charged NLC containing *Lavandula* or *Rosmarinus* can be proposed as a potential add-on strategy in the treatment of neurodegenerative diseases through intranasal administration, due to the well-known beneficial effects of essential oils and the mucoadhesive properties of the prepared NLC.

35. Dar Junaid Bashir et.al. 2022

In this study Dar Junaid Bashir et.al. reported oxidative stress has also been found to be involved in the proliferation of the disease. Magnoflorine is one of the active compounds of Coptidis Rhizoma and has high anti-oxidative properties. Active principle-loaded nanoparticles have shown increased efficiency for neurodegenerative diseases due to their ability to cross the blood−brain barrier more easily. An in vitro study involving magnoflorine-loaded chitosan collagen nanocapsules (MF-CCNc) has shown them to possess inhibitory effects against oxidative stress and to some extent on AChE as well. In the current study, both nootropic and anti-amnesic effects of magnoflorine and MF-CCNc on scopolamine-induced amnesia in rats were evaluated. The treatment was done intraperitoneally (i.p.) once daily for 17 consecutive days with MF-CCNc (0.25, 0.5, and 1 mg), magnoflorine (1 mg), and donepezil (1 mg).

36. Tanima Bhattacharya et.al., 2022

In this study Tanima Bhattacharya et.al., reported the promising application, and recent trends of combined nanotechnology and phytomedicine for the treatment of neurological disorders (ND) as compared to conventional therapies, have been addressed. Nanotechnology-based efforts performed in bioinformatics for early diagnosis as well as futuristic precision medicine in ND have also been discussed in the context of computational approach.

37. Kothamasu Pawankumar et.al., 2012

Nanocapsules possessing extremely high reproducibility have a broad range of life science applications. They may be applied in agrochemicals, genetic engineering, cosmetics, cleansing products, wastewater treatments, adhesive component applications, strategic delivery of the drug in tumors, nanocapsule bandages to fight infec¬tion, in radiotherapy and as liposomal nanocapsules in food science and agriculture. In addition, they can act as self-healing materials.The enhanced delivery of bio¬active molecules through the targeted delivery by means of a nanocapsule opens numerous challenges and opportunities for the research and future development of novel improved therapies.

38. Purohit Deepika et.al 2023

In the present review, our team made a deliberate effort to summarize the recent advances in the field of NCs and focus on new patents related to the implementation of NCs delivery systems in the area of some life-threatening disorders like diabetes, cancer, and cardiovascular diseases.

39. Mehandole A et.al., 2023

Amongst the several nano-drug delivery systems, lipid or polymer-based core-shell nanocapsules (NCs) have garnered much attention of researchers owing to its multidisciplinary properties and wide application. NCs are structured core-shell systems in which the core is an aqueous or oily phase protecting the encapsulated drug from environmental conditions, whereas the shell can be lipidic or polymeric. The core is stabilized by surfactant/lipids/polymers, which control the release of the drug. The presence of a plethora of biocompatible lipids and polymers with the provision of amicable surface modifications makes NCs an ideal choice for precise drug delivery. In the present article, multiple lipidic and

polymeric NC (LNCs and PNCs) systems are described with an emphasis on fabrication methods and characterization techniques.

40. Hamid-Reza Alipour et.al., 2022

Alzheimer's disease (AD) is a neurological disorder in which the neuronal degeneration is associated with inflammatory processes and oxidative stress. Since alpha-terpineol was shown to possess antioxidant and anti-inflammatory effects, the administration of this compound was studied on a rat model of AD. To create this model, Aβ1-42 was injected into the hippocampus of male Wistar rats. Generated AD models were divided into simple AD models and AD models in which short-term immobilization stress was added. *n vitro*, shorter fibrillar structures were formed in the presence of alpha-terpineol, which indicates an anti-amyloid effect for this compound. In conclusion, alpha-terpineol significantly counteracted AD consequences.

Hypothesis/Assumptions:

i) Proposed research work will fill gap of existing research wherein nanoparticles and different Nano formulations will be developed with improved stability & bioavailability.

ii) Proposed research work will fill gap of existing research of evaluating nanocapsules.

iii) Proposed research work will fill gap of existing research wherein novel dosage form would deliver the exact therapeutic effect.

Aim & Objective:

Alzheimer's disease is related with degeneration of cholinergic neurons in the basal forebrain that play a vital role in cognitive functions, including memory. As a result of such degeneration, patients suffering from the disease exhibit a marked reduction in acetylcholine synthesis, choline acetyltransferase activity, acetyl cholinesterase activity and choline uptake.

The early symptoms of the disease include forgetting recent events or conversations. As the disease progresses, a person with Alzheimer's disease will develop severe memory impairment and lose the ability to carry out everyday tasks. Medications may temporarily improve or slow progression of symptoms.

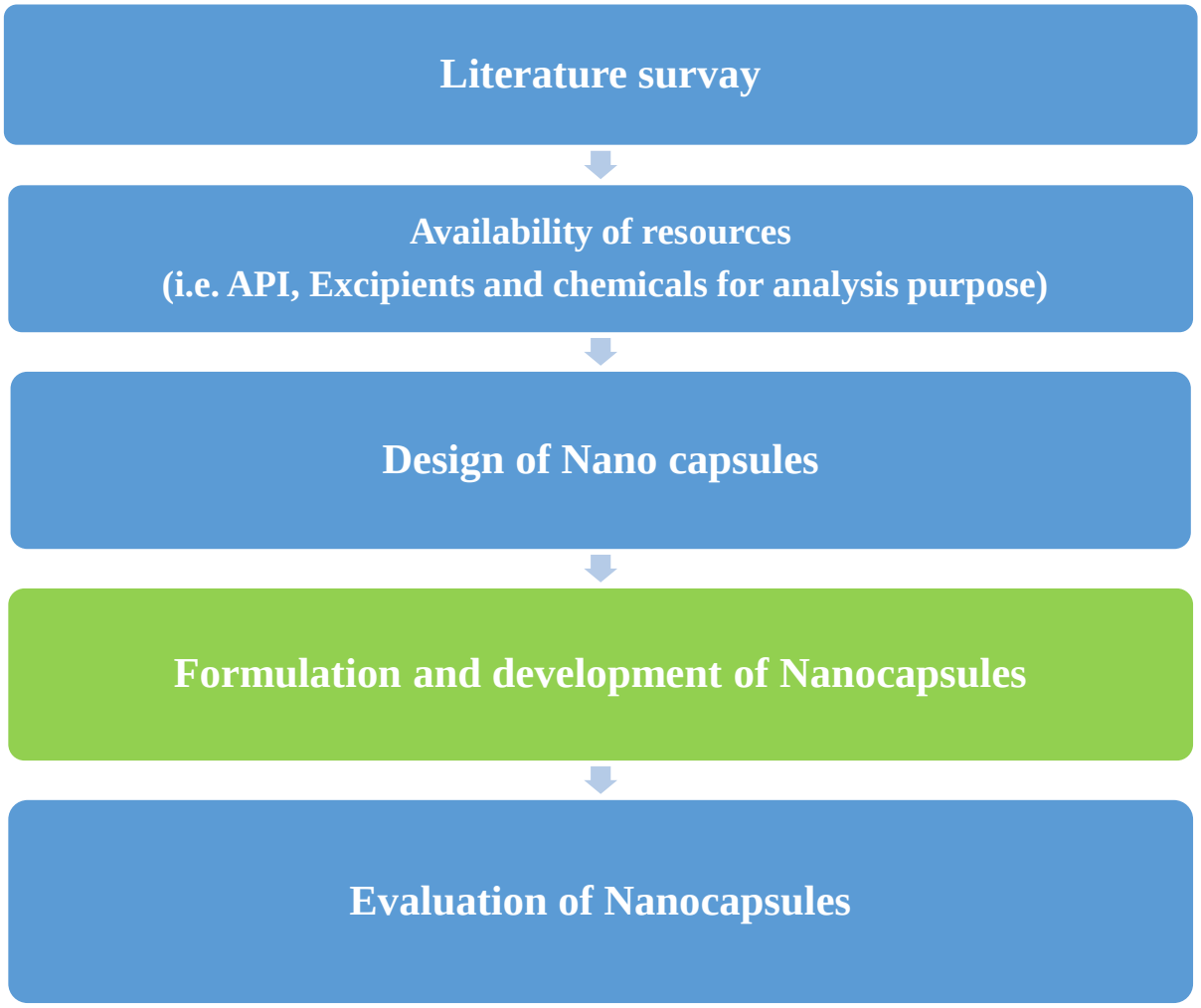
Many of the herbal drugs possess the anti-Alzheimer’s activity with less side effects when compared with the conventionally available synthetic drug.

 The aim of present study is to formulate nanocapsule of methyl Eugenol & terpineol and comparison of their neuroprotective activity.

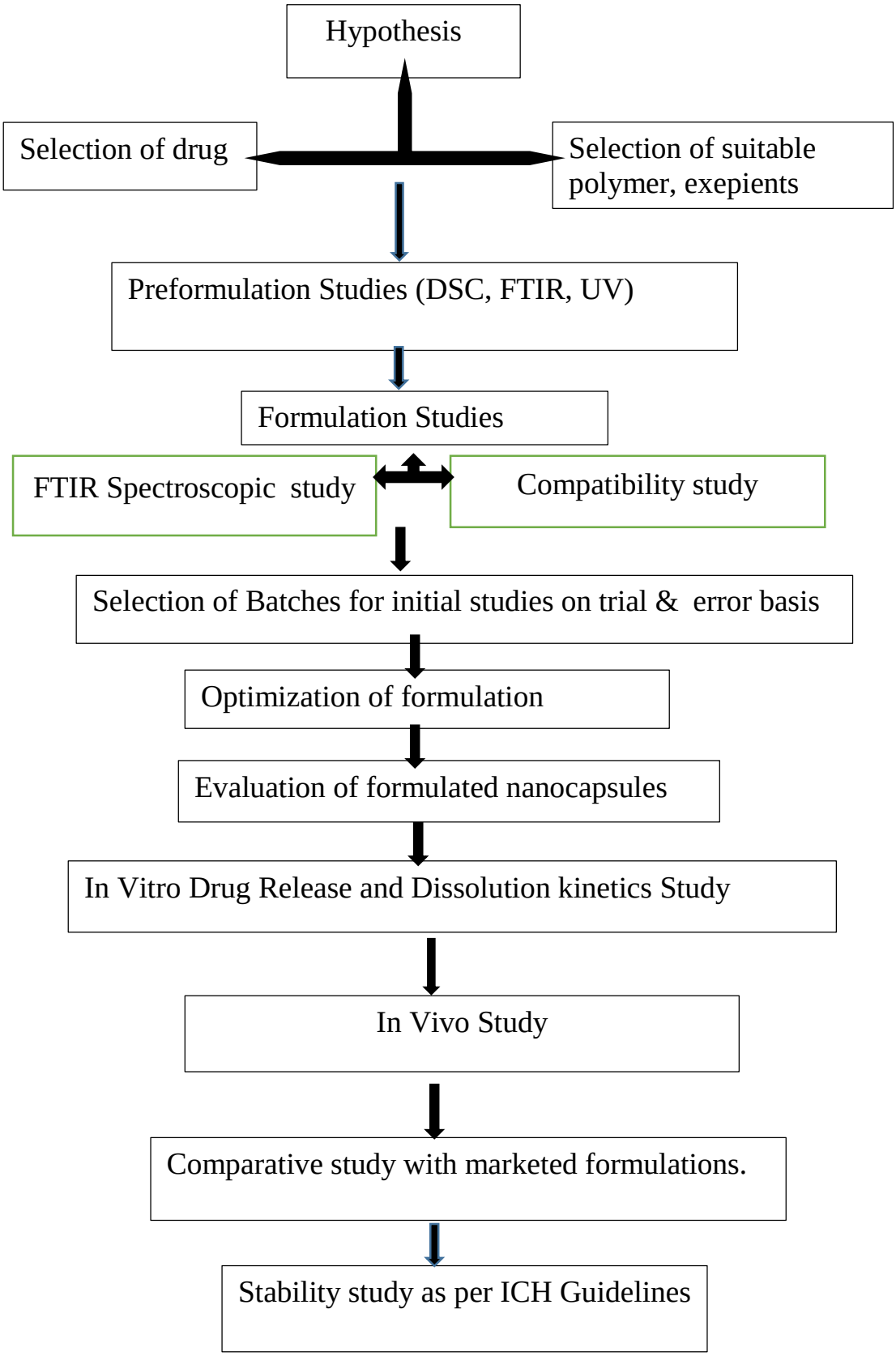
 The object of the present invention is to formulate a novel formulation from the essential oil that has anti-Alzheimer’s activity.

 To evaluate nanocapsules from different essential oil and study comparison of their neuroprotective activity.

Plan of Work


Literature survay
Availability of resources
(i.e. API, Excipients and chemicals for analysis purpose)
Design of Nano capsules
Formulation and development of Nanocapsules
Evaluation of Nanocapsules

METHODOLOGIES AND TECHNIQUES:


Hypothesis
Selection of drug
Selection of suitable polymer, exepients
Preformulation Studies (DSC, FTIR, UV)
Formulation Studies
FTIR Spectroscopic study
Compatibility study
Selection of Batches for initial studies on trial & error basis
Optimization of formulation
Evaluation of formulated nanocapsules
In Vitro Drug Release and Dissolution kinetics Study
In Vivo Study
Comparative study with marketed formulations.
Stability study as per ICH Guidelines

Formulation and evaluation of Nanocapsule

Materials

Organic phase- Acetone, ethyl acetate

Aqueous phase –Water

Polymer- Poly (ε-caprolactone), Eudragit S100, cellulose acetate, Poly lactic glycolic acid

Surfactant- Polysorbate 80, Tween 80, Span 60

1. Physicochemical characterization of nanocapsules

1.1. Particle size and zeta potential.

1.2. Quantification of XAN and 3-MeOXAN content in nanocapsules

1.3. Differential scanning calorimetry (DSC)

1.4. Morphological studies

1.5. Phytochemical Analysis

The Compound isolated was also confirmed by following spectral analysis**.**

1. UV-Visible Spectroscopy
2. Infrared Spectroscopy
3. Nuclear Magnetic Resonance Spectroscopy (NMR)
4. Mass Spectrometry for Chemical Compounds Identification

2. Preparation of Nano capsules

3. In vitro release studies Nano capsules

4. In vivo study

5. Physical stability

6. Morphological studies

7. Compare with marketed preparation

8. Data compilation and thesis writing

Significance of proposed problem:

Some major advantages of nanocapsule is their high surface-area-to-volume ratio, chemical and geometric tunability, and they have the ability to interact with biomolecules to facilitate uptake across the cell membrane. The surface area also has a large affinity for drugs and small molecules, like ligands or antibodies, for targeting and controlled release purposes. Nanoparticles refer to a family of materials both organic and inorganic. Each material has uniquely tunable properties and thus can be selectively designed for specific applications like:

1. Crossing the blood brain barrier (BBB) in brain diseases and disorder.
2. Enhancing targeted intracellular delivery to ensure the treatments reach the correct structures inside the cell.
3. Combining diagnosis and treatment.

Is it possible to formulate the formulation using essential oil?

Yes, the proposed research work focused only on development of novel dosage form.

Will novel dosage form meet unmet needs of the formulation being as safe as effective when compared with existing marketed dosage form? And how it will be ensured?

Yes, the proposed novel dosage form would be as safe as effective when compared to existing marketed dosage form and it would ensure through thorough development and performing the stability studies as well as in-vitro, in-vivo relation.

Expected outcome:

1. This will meet the unmet needs of stability enhancement of essential oils for 3-4 month and increase the oral compatibility.

2. Ease of manufacture and scale- up is one of the most important advantages that make Nanocapsules unique when compared to other drug delivery systems like Nano sphere, liposome, nanoparticles, etc., as they require very simple and economical manufacturing facilities like simple mixer with agitator and volumetric liquid filling equipment for large-scale manufacturing. This explains the interest of pharmaceutical industry in the nanocapsules.

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Ms. Pradnya Karbhari Pehere

Signature of the Research Scholar

Dr. Dharmendra Ahuja

Signature of the Research Guide